UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,949	01/07/2002	Kazuhiro Nakashima	0397-0438P	6273

2292 7590 06/14/2005

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,949	NAKASHIMA ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-10,13 and 14* is/are rejected.

7)☒ Claim(s) *5-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed February 7, 2005 is acknowledged and has been entered. Claims 1-10, 13, and 14 have been amended. Claims 11 and 12 have been added. Accordingly, claims 1-10, 13, and 14 are pending.

Applicant's amendment filed February 18, 2005 is also acknowledged and has been entered. Claim 1 has been amended. Currently, claims 1-10, 13, and 14 are pending and remain under examination.

Rejections Withdrawn

2. All rejections not reiterated herein have been withdrawn.

3. The rejections of claims 11 and 12 are now moot in light of Applicant's cancellation of the claims.

4. In light of Applicant's amendment, the rejection of claims 1, 2, 9, and 10 under 35 U.S.C. 102(e) as being anticipated by Moskowitz et al. (US 2001/0046685), is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, is indefinite in being incomplete for omitting essential structural and functional cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. Specifically, it is unclear how the distinguished and counted unagglutinated insoluble carrier particles, agglutinated insoluble carrier particles, and blood cells, correlate to the elements, i.e. target antigen or target antibody, in the preamble so as to allow assaying for target antigen or target antibody, as required by the preamble. For example, does the amount of agglutinated insoluble carrier particles provide a concentration of the target antibody or target antigen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 13 and 14 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Kosako (US Patent 5,527,714) for reasons of record.

Kosako discloses an immunoassay apparatus comprising flow cell having a mixing (agitating) part and dispensing mechanism for presenting a reaction mixture to

the flow cell, a laser for irradiating particles through a flow cell, a detector (photo acceptance unit) for detecting scattered light, a signal processing means having a microcomputer for converting the light signal into an electrical signal for analysis and measurement of stored digital values and for setting threshold values for distinguishing particle size distribution between agglutinated particles and unagglutinated particles. The detector is connected to an amplifier where electrical signal is converted to a digital message by an A/D converter (see column 3, lines 14-51, column 5, lines 1-18, and column 6, lines 1-15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kosako (US Patent 5,527,714) in view of Moskowitz et al. (US 2001/0046685).

Kosako discloses an immunoassay comprising mixing an analyte sample with insoluble carrier particles sensitized with antibody, agitating the reaction mixture, subjecting the resulting immune agglutination reaction mixture including both agglutinated and unagglutinated particles to irradiation with laser, then nephelometrically detecting scattered light generated therefrom. The degree of agglutination is measured, and total particle size distribution curve is plotted including predetermined threshold values of unagglutinated particles, agglutinated particles, and spurious particles. The total resultant particles plotted in the distribution curve include agglutinated particles, unagglutinated particles, and other (spurious) particles wherein a first size distribution of the total particles and a second size distribution of spurious particles are determined and subtracted from the first distribution to produce a corrected size distribution of insoluble particles; hence, correcting for the concentration of analyte (antigen or antibody). Therefrom, the actual concentration of antigen or antibody is obtained (see column 3, lines 27-41 and claim 1).

Kosako differs from the instant invention in failing to disclose that the analyte sample is whole blood and the spurious particles are blood cells.

Moskowitz et al. disclose an immunoassay comprising mixing a whole blood sample with insoluble carrier particles (matrix) having antigen or antibody (fibrinogen or antibody to platelet cell surface glycoprotein receptor) immobilized thereto, subjecting the resulting immune agglutination reaction mixture including both agglutinated and

unagglutinated particles) to irradiation with laser light in the infrared region, then detecting scattered light generated therefrom. A control value is used in setting a base value (threshold value) for distinguishing unagglutinated particles from agglutinated particles and a standard calibrator is used to provide a standard curve for comparison with test results. The degree of agglutination is related to the concentration of antigen or antibody in the whole blood sample. The degree of agglutination is platelets is also determined and related to the number of platelets (blood cells) (see page 6, column 2 [0069] to page 7, column 2 [0071]) and column 8 [0080]). Extent of agglutination is measured nephelometrically (light scatter) (see page 8 [0079]). The insoluble carrier particles are at least about 0.1 um – 10 um (see page 3, column 1 [0035-0039]). Desirably, the immunoassay is performed at a temperature of at least 25 °C and in the range of 30 °C-40 °C and read at a time within 10 seconds to 5 minutes (see page 8, column 1 [0078] and column 2 [0087]). Confirmation of results has been confirmed by flow cytometry (see Figure 4 and page 10, column 1 [0123]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teaching of Steel into the nephelometric method of Kosako as modified by Moskowitz because Steel specifically taught application of forward angle scatter measurements in detecting agglutination formation or degrees thereof, and both of Kosako and Moskowitz teach nephelometric assays involving distinguishing between particle sizes in agglutination reactions and light scatter measurements.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kosako (US Patent 5,527,714) in view of Moskowitz et al. (US 2001/0046685) as applied to claims 1-3 and 9-12 above, and further in view of Steel et al. (WO 98/20351).

Kosako and Moskowitz et al. have been discussed supra. Kosako and Moskowitz et al. differ from the instant invention in failing to teach that the scattered light is a forward scattered light.

Steel et al. provide that certain agglutination assays use optical flow particle analyzers that detect agglutination formation or the degree of non-agglutination by measuring forward scattered light and using particles having different sizes (see page 2, lines 6-14).

One of ordinary skill in the art at the time the invention was made would have been motivated to measure forward scattered light as taught by Steel in the nephelometric assays taught by Kosako as modified by Moskowitz for measuring degrees of agglutination because Steel specifically taught that forward scattered light has the advantage of measuring different sizes of particles and aggregation formation in an assay mixture.

Response to Arguments

9. Applicant's arguments filed February 7, 2005 have been fully considered but they are not persuasive.

A) Applicant argues that Kosako does not anticipate claims 13 and 14 because Kosako does not disclose an immunoassay apparatus wherein an immunoassay can be carried out with a whole blood sample.

In response to Applicant's argument that the apparatus is not an immunoassay apparatus upon which an immunoassay can be carried out with a whole blood sample, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). In this case, Kosako specifically teaches the immunoassay apparatus as claimed, comprising a flow cell having a reaction part (mixing/agitating part), a dispensing mechanism for presenting a reaction mixture to the flow cell, a laser for irradiating particles through the flow cell, a detector (photo acceptance unit) which is connected to an A/D converter for detecting scattered light, a signal processing means having a data processing means (microcomputer) for converting the light signal into electrical signal for analysis and measurement of stored digital values and for setting threshold values for distinguishing particle size distribution between agglutinated particles and unagglutinated particles.

B) Applicant argues that claims 13 and 14 are not anticipated by Kosako because Kosako fails to disclose some elements of the claim, i.e. laser, photo acceptance unit, signal processing means, and data processing means, which are comprised in the immunoassay apparatus of the present invention.

Contrary to Applicant's argument, Kosako indeed, teaches the immunoassay apparatus as claimed, including a laser for irradiating particles through a flow cell, a detector (photo acceptance unit) which is connected to an A/D converter for detecting scattered light, a signal processing means, and a data processing means (microcomputer) for converting the light signal into an electrical signal for processing and analysis in column 3, lines 14-51, column 5, lines 1-18, and column 6, lines 1-15.

C) Applicant argues that the combination of Kosako with Moskowitz does not teach or suggest the claimed invention because neither, alone or in combination, disclose first and second threshold values as recited in the claimed invention, wherein the unagglutinated insoluble carrier particles can be distinguished from agglutinated insoluble carrier particles, or that the agglutinated insoluble carrier particles can be distinguished from blood cells, and that counting the particles or blood cells can be based on the set thresholds.

In response, the combination of Kosako with Moskowitz indeed, suggest the claimed invention because Kosako provides measuring and setting thresholds for degrees of agglutination of the insoluble particles, wherein total particle size distribution curve is plotted including predetermined threshold values in order to distinguish

between unagglutinated particles, agglutinated particles, and spurious particles. The total resultant particles plotted in the distribution curve include agglutinated particles, unagglutinated particles, and other (spurious) particles wherein a first size distribution of the total particles and a second size distribution of spurious particles are determined and subtracted from the first distribution to produce a corrected size distribution of insoluble particles; hence, correcting for the concentration of analyte (antigen or antibody). Moskowitz et al. is incorporated herein, only for the teaching of using whole blood in a nephelometric immunoassay wherein whole blood sample is mixed with insoluble carrier particles having antigen or antibody immobilized thereto, subjecting the resulting immune agglutination reaction mixture including both agglutinated and unagglutinated particles, to irradiation with laser light in the infrared region, then detecting scattered light generated therefrom. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute whole blood as taught in the method of Moskowitz into the method of Kosako wherein agglutinated portion, unagglutinated portion, and spurious particles are taken into account for accuracy of nephelometric assay results because use of whole blood in the agglutination assay of Moskowitz has the advantage of less sample handling and the Kosako reference which appears to be generic in the type of analyte mixture used provides significant improvement in assaying for analyte in a heterogeneous sample such as whole blood.

D) Applicant argues that the combination of Kosako and Moskowitz with Steel does not teach or suggest the claimed invention because Steel does not cure the deficiencies of Kosako and Moskowtiz wherein neither one, alone or in combination, disclose first and second threshold values as recited in the claimed invention, wherein the unagglutinated insoluble carrier particles can be distinguished from agglutinated insoluble carrier particles, or that the agglutinated insoluble carrier particles can be distinguished from blood cells, and that counting the particles or blood cells can be based on the set thresholds.

In response, the combination of Kosako with Moskowitz indeed, suggest the claimed invention because Kosako provides measuring and setting thresholds for degrees of agglutination of the insoluble particles, wherein total particle size distribution curve is plotted including predetermined threshold values in order to distinguish between unagglutinated particles, agglutinated particles, and spurious particles and Moskowitz et al. teaches application of whole blood in a nephelometric assay wherein whole blood sample is mixed with insoluble carrier particles having antigen or antibody immobilized thereto, subjecting the resulting immune agglutination reaction mixture including both agglutinated and unagglutinated particles, to irradiation with laser light in the infrared region, then detecting scattered light generated therefrom. Steel is incorporate herein, only for the teaching of using forward scattered light in detecting particles in the flow cell. Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teaching of Steel into the nephelometric method of Kosako as modified by Moskowitz because Steel specifically

taught application of forward angle scatter measurements in detecting agglutination formation or degrees thereof, and both of Kosako and Moskowitz teach nephelometric assays involving distinguishing between particle sizes in agglutination reactions and light scatter measurements.

Prior Art

10. Claims 5-7 are clear of the prior art. Claims 5-7 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

11. Applicant's submission of the requirements for the joint research agreement prior art exclusion under 35 U.S.C. 103(c) on February 7, 2005 and February 18, 2005 prompted the new grounds of rejection under 37 CFR 1.109(b) presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.02(l)(3). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
June 7, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
06/10/05